Editorial Comment

More on Polymyalgia Rheumatica and Giant Cell Arteritis

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Elsewhere in this issue Healey and Wilske review recent data on polymyalgia rheumatica and giant cell arteritis based on their own extensive experience and reports in the literature. They point out that even though Horton had described cases of temporal arteritis as early as 1932 and that the European literature reported cases of polymyalgia rheumatica under several different names, both conditions were considered uncommon in this country before the mid 1960s. They raise the question whether these conditions were merely poorly recognized in the United States in earlier years or whether there has been a change in the frequency of these diseases to account for the high incidence rates that have been described in some recent surveys.

In the Olmsted County, Minnesota, epidemiologic study of giant cell arteritis, incidence rates could be calculated over time and the change documented.[1] The rates increased more than three times from 5.1 per 100,000 persons older than 50 years of age in the first decade surveyed (1950 to 1959) to 17.4 cases per 100,000 persons in the last five years of the study (1970 to 1974). The prevalence of active and resolved cases at the beginning of 1975 was 133 per 100,000, that is, about one case in every 750 persons older than 50 years. Somewhat similarly, the prevalence of polymyalgia rheumatica increased 22% in the second five-year segment (1975 to 1979) of the ten-year Olmsted County study.[2] An estimated prevalence of active and resolved cases of polymyalgia rheumatica at the beginning of 1980 was about 500 per 100,000 persons older than 50 years, or 1 person in 200.

Healey and Wilske note some recent descriptions of the diverse guises in which giant cell arteritis may present, such as depression, anemia and fever of unknown origin with shaking chills, which may not directly suggest the underlying nature of the disease.[3] Such reports aid in identifying occult cases. In addition, the characteristics of aching and morning stiffness of polymyalgia rheumatica are also better recognized. Although objective findings are not prominent in cases of polymyalgia rheumatica, careful examination may show, in addition to small knee effusions, slight swelling or tenderness of several other joints and limitation of active and passive motion of the shoulders and hips. In severe cases of longer duration, disuse muscle atrophy of the shoulders may become clearly evident. Radiographic changes of joint damage have been seen occasionally, also supporting the idea that synovitis is an important cause of the musculoskeletal pains.[4] In fact, in a small number of patients persistent synovitis eventually may permit a diagnosis of seronegative rheumatoid arthritis.

It is clear that cases of polymyalgia rheumatica did occur before the 1960s. At our own institution, for example, polymyalgia rheumatica went under the name of "secondary fibrositis" and was considered a moderately common process but it was not studied thoroughly.

The final answers on the questions of changing incidence or better recognition remain to be given, but I suspect that much of the "change" is better awareness nowadays of both conditions, plus a predisposition toward them of certain populations. If improved recognition is the cause of the increasing incidence rates, the rates should begin to level off as maximum awareness is reached. A recent occurrence at our institution suggests that a good level of awareness by many doctors is being approached. An internist member of the Infectious Disease Division was evaluating a patient with a fever of unknown origin and asked a general surgeon to see the patient with a view toward a possible abdominal exploration to further investigate the cause of the fever. The surgeon looked over the data and asked the internist whether he had thought of the possibility of giant cell arteritis even though no headache or visual symptoms were present, and would consider a temporal artery biopsy before going to the abdominal exploration!

Other factors, such as genetic or even climatic, may also influence the incidence of these conditions. As has been pointed out, giant cell arteritis is most common in whites. A relationship with the antigen HLA-DR4 has been noted by several authors. Identical twins and multiple family members with these conditions have

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also been reported, but the meaning of this has yet to be completely determined.

Smith, Fidler and Pinals studied the epidemiology of giant cell arteritis in Shelby County, Tennessee, an urban population in South Central United States.[5] Over a ten-year period (1971 to 1980), 26 cases were identified, producing an average annual incidence of 1.58 per 100,000 persons aged 50 years and older. The incidence was seven times greater in whites than in blacks. But the overall incidence was considerably lower than recorded in Olmsted County[2] and also in Scotland[6] and Sweden.[7] The authors felt that the differences between their findings and those of others could be accounted for only in part by racial distribution. Assuming good case ascertainment by Smith and coworkers, a potential role for climate or other environmental influences needs to be considered. Similar studies in other southern locations or other geographic areas should be carried out to place the various studies in perspective and to search for factors that may have etiologic significance.

As pointed out by Healey and Wilske, the artery lesions appear to focus on elastic tissue, but no direct evidence of an immunologic reaction to elastic tissue has been obtained. In addition to the work cited by Healey and Wilske, we have looked for antibodies to elastic tissue in serum specimens from patients with giant cell arteritis (J. M. Peterson and G. G. Hunder, MD, unpublished observations). An assay was used in which patients' serum was mixed with purified, denatured, finely particulate and insoluble human aortic elastin. After adding the patient serum, the elastin was washed and mixed with ^{131}I-labelled staphylococcal A protein to detect IgG antielastin antibodies. No antibodies were found in serum specimens from 15 patients, though one of ten serum specimens from patients with lupus erythematosus did have elevated antibody titers, as did serum from guinea pigs that were immunized against human elastin. A search for antibodies to native elastin might yield different results.

It is to be hoped that improved methods of diagnosis will be developed to help determine whether patients with somewhat similar, but not typical, symptoms also have these diseases. Use of the workshop standards for defining polymyalgia rheumatica should help make study results more comparable from one center to another, especially since no diagnostic test for polymyalgia rheumatica is available. The fact that heavy emphasis is placed on the erythrocyte sedimentation rate in the recognition of polymyalgia rheumatica indicates a need for better tests. Furthermore, it should be remembered that polymyalgia rheumatica as well as giant cell arteritis may occur in association with a normal or near-normal erythrocyte sedimentation rate. The frequency of this is not known but probably occurs in about 1% of those with giant cell arteritis and slightly more often in cases of polymyalgia rheumatica. The availability of baseline erythrocyte sedimentation rates before a patient became ill may help evaluate current tests.[2] Other acute-phase reactant blood proteins such as C-reactive protein, fibrinogen, α_2-globulins and the like have been used to follow patients but have not been shown to be significantly better than the erythrocyte sedimentation rate in this regard. Nevertheless, these tests can be used in conjunction with the sedimentation rate to help evaluate the status of patients.

On the other hand, in giant cell arteritis a positive finding on a temporal artery biopsy specimen is diagnostic. Opinions on the clinical usefulness of doing temporal artery biopsies when giant cell arteritis is suspected have varied considerably. Wilske and Healey point out instances of patients who had no abnormalities on a temporal artery biopsy but in whom symptoms of giant cell arteritis later developed and, conversely, patients with polymyalgia rheumatica who had no symptoms of arteritis but who had a biopsy in which the specimen showed giant cell arteritis. Other authors have suggested that when the diagnosis seems clear on a clinical basis, a biopsy is superfluous, and in cases where the clinical picture is obscure, a patient may be treated despite the absence of abnormalities on a biopsy. Therefore, the argument sometimes goes, biopsies are not usually required. In addition, a patient may need a superficial temporal-middle cerebral artery bypass operation at some time in the future and the temporal artery should be saved in anticipation.

Now, two studies have evaluated the efficacy of temporal artery biopsy. In one, 193 temporal artery biopsies were done over the 10-year period, 1968 to 1978.[8] In 28, the biopsy specimens showed arteritis. Follow-up information was available for at least two years after the biopsy in 91 of these, including the 28 with positive findings and 63 with negative findings. Only three cases in which results of a biopsy were negative (5%) were diagnosed as temporal arteritis. One of the patients died five months after the biopsy and was found to have temporal arteritis at autopsy. The other two patients were felt to have temporal arteritis clinically at the time of biopsy. No biopsy-related complications were noted immediately or found in the follow-up. The authors suggested that a biopsy may be done of the frontal branch of the superficial temporal artery if there is concern about the need for a temporal-middle cerebral artery bypass operation in the future, as the parietal branch is usually preferred for this procedure. None of their patients were noted to need such treatment.

In the second study, all 134 residents of Olmsted County who had temporal artery biopsies over the 15-year period (1965 to 1980) were followed.[9] Initially the biopsy specimens showed positive findings in 46 cases and negative in 88. No complications from the biopsy procedure were observed and in none has a question yet come up about the need for a bypass surgical procedure. There was a close similarity between biopsy-positive and biopsy-negative groups in overall presenting clinical features, with almost equal frequencies of polymyalgia rheumatica, fever, headaches and visual disturbances including blindness. Two findings, however—jaw claudication and clinical ab-

normalities of a temporal artery—were significantly more common in patients in whom the biopsy specimen showed giant cell arteritis. A history of jaw pain or claudication was found in 54% of the biopsy-positive group, but in only 3% of the patients who had normal biopsy results. A clinically abnormal temporal artery was present in 67% of those in whom biopsy results were positive, which was more than twice as common as in those in whom abnormalities were found on biopsy. Jaw pain or abnormal temporal arteries, or both, were present in 78% of those with positive biopsy results. Over a median follow-up of 70 months, only 8 of the 88 biopsy-negative patients had clinical courses requiring long-term, high-dose corticosteroid therapy for giant cell arteritis. In these eight, a diagnosis of giant cell arteritis was made during follow-up on the basis of an additional temporal artery biopsy, autopsy examination, angiographic studies or the development of convincing clinical evidence. To put these findings in terms of efficacy of biopsy, it could be stated that the initial temporal artery biopsy correctly predicted the subsequent need for corticosteroid therapy in 94% of cases (46 plus 80/134). A temporal artery biopsy that showed no abnormalities accurately predicted that high-dose corticosteroid therapy was not needed in 91% (80/88). These figures compare well with most tests available today and indicate that temporal artery biopsy should be done before patients are committed to high-dose, long-term corticosteroid therapy. The high predictive value of findings on a temporal artery biopsy in this study may be due in part to our practice of taking a large biopsy specimen and frequently carrying out bilateral biopsies when examination of frozen sections of the first side shows no abnormalities. In this study, 15 of the 46 initially positive biopsies were bilateral and 49 of the 88 negative biopsies were bilateral. If a temporal artery is clearly abnormal clinically, only a small segment need be removed for histologic examination; but if the arteries are not clearly abnormal a larger segment, 3 to 6 cm in length of one or of both sides, should be taken for examination because the arteritis frequently does not affect all portions of the artery and identification of affected areas may be found only after an examination of many sections.

The question of whether to do a temporal artery biopsy in a patient with polymyalgia rheumatica who has no vascular-related symptoms or signs may be more difficult because, as pointed out, some have arteritis. On the assumption that arteritis is unlikely, such patients tend to be treated with nonsteroidal anti-inflammatory drugs or low doses of corticosteroids, which would ameliorate musculoskeletal pain and cause fewer drug side effects but might not prevent vascular complications should giant cell arteritis be present. My clinical experience with these cases suggests that patients with milder disease, especially early in the course of the illness, or those whose symptoms have been present for longer than a year may be carefully followed without a biopsy. The chance of vascular complications in such patients is quite low though not accurately known. An estimate may be roughly calculated by considering that temporal artery biopsy will show giant cell arteritis in about 15% to 20% of patients with polymyalgia rheumatica without symptoms or signs of giant cell arteritis. Of those with arteritis, vascular complications might occur in perhaps 20% to 40% if not treated. Thus, patients with polymyalgia rheumatica lacking findings of giant cell arteritis might have vascular complications in a frequency of 3% to 8%. If such patients are treated with low doses of corticosteroids and all symptoms resolve and the laboratory tests return to normal, vascular occlusions or ruptures probably will not occur regardless of the nature of the underlying disease. The problem of not doing a biopsy before treatment arises in interpreting the meaning of a persistently elevated sedimentation rate and only partial resolution of the anemia, though musculoskeletal pains have lessened, after starting therapy at low or moderate corticosteroid doses.

As noted by Healey and Wilske, most patients with giant cell arteritis respond rapidly to corticosteroid treatment. The optimal dose probably differs from patient to patient. Because a chance of irreversible damage from a vascular occlusion or rupture is present, it has been the usual practice to give large initial doses as suggested, even though they may be higher than necessary in some patients. On the opposite side, a small percentage of patients with giant cell arteritis do not respond as readily to corticosteroids, and high doses given over a longer period regularly result in osteoporosis of the spine with compression fractures or other complications. The reason for this occasional lack of response is not apparent and such patients are indistinguishable from responsive patients regarding pretreatment symptoms and histopathologic findings. These cases pose a difficult problem because no other drugs have been shown to be clearly effective in the treatment of this disease. Cyclophosphamide, azathioprine, dapsone and a variety of other medications all have been reported as being useful; however, the experience with these medications is anecdotal and no control studies have been reported. Nevertheless, if pronounced hypercortisonism develops in a patient after several months of high-dose prednisone therapy, consideration can be given to starting one of these drugs such as cyclophosphamide if evidence of clinical activity is obvious.

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